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Intravenous Administration Issues

A Comparison of Intravenous Insertions and Complications in Vancomycin Versus Other Antibiotics

ABSTRACT
Nurses on a surgical unit compared 2 groups of patients, vancomycin versus other antibiotics, to determine whether vancomycin intravenous therapy is associated with more peripheral intravenous (PIV) complications. Data were collected on a number of PIV attempts and insertions, phlebitis and infiltration scores, nursing time, and missing or late doses on 153 orthopedic and trauma patients. Increased adverse outcomes were found with repeat venipunctures, attempts, nursing time, and infiltration. Patients receiving vancomycin through a PIV catheter developed more complications than those receiving other antibiotics. This is increasingly important because nurses make recommendations for vascular catheters.

Many factors contribute to the growing numbers of patients with vascular depletion.[1] One factor is the use of intravenous (IV) vancomycin, a valuable, powerful antibiotic with a pH less than 4. With the increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), coagulase-negative *Staphylococcus* species, *Clostridium difficile*, and methicillin-resistant *Staphylococcus epidermis* (MRSE), clinical nurses face more patients with infections who require vancomycin therapy, the preferred drug of choice to combat these organisms.[2,3] Because vancomycin is one of the most acidic IV antibiotics, and consequently one of the most damaging to patients' veins,[4] and long-term therapy lasts weeks or months, there is an urgent need to assess cost and complications of its administration.

Ensuring reliable access is critical for reaching optimal outcomes, including decreasing costs of care and length of stay for patients. Intravenous therapy is common among hospitalized patients because of the increasing complexity of disease processes. Nurses typically insert peripheral intravenous (PIV) catheters in patients and are responsible for interventions related to assessment and monitoring of the site. In addition, nurses administer medications and infusions via PIV catheters, so they are often first to document problems. Consequently, staff nurses are involved in discussions with the interdisciplinary team to communicate PIV site outcomes and recommendations on IV therapy.

With the increased administration of IV vancomycin, nurses report a greater incidence of PIV complications and more patient care time spent on repeated attempts to insert PIV catheters, yet these perceptions have not been formally documented. The purpose of the study was to compare and quantify adverse outcomes between 2 groups of surgical patients with peripheral catheter insertions: those receiving vancomycin versus those receiving other antibiotics.

BACKGROUND

Chemistry

Since vancomycin has a pH less than 4, no matter how dilute or how fast it is delivered, vancomycin damages the veins and can cause serious extravasation injuries and phlebitis.[1,4-6] Blood dilutes and neutralizes the vancomycin. Because the blood flow in a central vein is more powerful, it flushes the vancomycin from the vein wall before complications arise. Therefore, the Infusion Nurses Society (INS) recommends central catheters for vancomycin and low-pH antibiotic infusions.[7] Whether a patient receives a PIV or central catheter, however, is

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The authors have disclosed that they have no financial relationships related to this article.

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a clinical decision that requires weighing the benefits and risks of both routes of drug administration.

For the purposes of this discussion, infiltration and extravasation are the accidental administration of solution or medication into the tissues surrounding the IV catheter.[5] Infiltration specifically involves solutions or medications that are nonvesicant, and extravasation occurs with vesicant solutions or medications.[5] "*Vesicant* refers to any medication or fluid with the potential for causing blisters, severe tissue injury, or necrosis if it escapes from the vascular pathway."[5] Vancomycin and other low-pH antibiotics, as well as those high in osmolarity (≥600 mOsm/L), are considered vesicant infusions.[1]

Peripheral Intravenous Catheters: Risk and Benefits

Benefits of PIV catheters include low cost and ease of access; clinical staff nurses insert PIV catheters in the patient's room at any hour of the day or night. PIV venipunctures are potentially painful, and veins are damaged by infiltration, extravasation, and phlebitis, and, rarely, bloodstream infections (BSIs).[8] Complications from infiltration, extravasation, and phlebitis can range from pain and redness at the site to damage requiring surgical repair and loss of function.

Phlebitis is the most frequent complication of PIV insertions. Uslusoy and Mete[9] determined that 54.5% of 568 PIV catheter sites developed phlebitis. Maki and Ringer[10] reported that phlebitis occurred in 41.8% of catheter insertions studied and found that antibiotic therapy was the single highest predictor of phlebitis in the 1054 catheter samples. In addition, Lanbeck et al[11] found that 1 of every 5 patients with a PIV catheter with antibiotics administration developed phlebitis. Scales[12] showed an increase in BSIs for PIV insertions; although BSI rates with PIV catheters are low, the frequency of PIV catheter use results in annual morbidity.[13] Other problems identified with PIV administration of medications are delayed and missing doses while waiting for vascular access.

Central Catheters: Risks and Benefits

To prevent these complications for vesicant infusions requiring long-term therapy or frequent doses, central vascular access is the preferred and recommended method of administration.[6,13] Central catheter insertion requires a higher level of skill and a surgical field-type environment; consequently, a catheter insertion incurs higher costs. In addition, central catheters dispose the patient to complications with greater negative impact than peripheral catheters, including infection, thrombosis, pneumothorax, and air embolism. Complications are more serious when they occur in a central catheter than in a PIV catheter.[12]

Increasing numbers of central catheter infections are seen among patients in intensive care units (ICUs) versus acute care floors or ambulatory settings.[13] In its report on "Guidelines for the Prevention of Intravascular Catheter-Related Infections," the Centers for Disease Control and Prevention estimated 250,000 annual catheter-related infections from central vascular catheters for both adult and pediatric patients.[14] However, "specialized IV teams have shown unequivocal effectiveness in reducing the incidence of catheter-related infections and associated complications and costs."[13(p5)]

To combat the increasing numbers and cost of BSIs related to central vascular catheters, the Institute for Healthcare Improvement included the evidence-based "Central Line Bundle" as part of the *100,000 Lives* campaign.[14,15] The BSIs resulting from central catheters are primarily due to length of time patients are in the ICU, multiple drug treatments required for their diagnosis, site selection, hand hygiene, skin antisepsis, and insertion during emergency situations.[13,14] Since the Central Line Bundle has been implemented throughout multiple healthcare institutions across the United States, BSIs from central vascular catheters have decreased.[14] Estimated costs of a BSI from a central catheter occurring within an ICU or acute care floor range from $3700 to $29,000.[15,16]

Fear of infection, a dangerous and costly adverse outcome, is a major reason for not inserting a central catheter. It is recommended that central catheters should be removed when no longer necessary to prevent complications.[12] If central catheter infections ensue, costs are not reimbursed as regulated by the Centers for Medicare & Medicaid Services nonpayment initiative CMS-1533-FC, effective October 1, 2008.

Additional Considerations

A PIV catheter costs about $45, assuming 1-time insertion success; this includes cost of a start kit, catheter, saline flush syringe, extension set with clave, and 20 minutes of nursing time. For peripherally inserted central catheters (PICCs), the cost varies widely on the basis of the type of catheter placed. The cost of a PICC placement to the hospital (including chest radiograph) is approximately $350 to $400 (K. King, e-mail, September 9, 2009). These costs do not take into account patient satisfaction, increase or decrease in length of stay, and delays in therapy due to lost access. In addition, PICCs are contraindicated in orthopedic patients who need crutches to walk because of the placement through the upper arm. Furthermore, there is evidence that interoperative and short-term (<48 hours) postoperative dosing of antibiotics is effective.[17] Thus, care providers are hesitant to order central catheters; in some cases, the cost of central catheter insertion may outweigh its benefits.

METHODS

Design and Setting

The researchers used a nonrandomized, comparative design to determine whether there was a significant difference in complications between 2 groups: patients with peripheral access receiving vancomycin versus patients with peripheral access receiving other antibiotics with a pH of less than 4. A full power analysis was run with a recommendation for 2 groups of 64 patients. The study was conducted on a 32-bed surgical unit in a Southeastern academic medical center that staffs approximately 50 RNs. Each patient who received antibiotics for more than 24 hours was eligible for the study. To maintain confidentiality, each eligible patient was given a research number written on the data collection tool. The institutional review board and the hospital's nursing research committee reviewed and approved the project.

The research tool was a columned chart that was placed in a folder outside the patient's room. Definitions for the values requested were determined. Measures included the following variables:

- Phlebitis and infiltration scores (1-5 per INS guidelines)
- Number of repeat PIV insertions (venipunctures) while on antibiotics
- Number of attempts to get a successful PIV insertion. An *attempt* was defined as piercing the surface of the skin to insert a PIV catheter
- Nurses' time in room for starting the PIV catheter
- Delayed doses due to PIV venipunctures (time from scheduled to actual medication)

Nursing time in room was the time it took a nurse to find a vein and insert a PIV catheter; however, researchers anticipated problems with estimating insertion times. Therefore, the nurses timed 5 PIV insertions and decided a 10-minute default was a conservative value to capture time in the room when there were no data for time in room.

After nurses administered a dose of antibiotic, they recorded information on the bedside collection tool. Data collection started when the antibiotics were first given on the unit. If transferred from another unit,

TABLE 1
Outcomes and Descriptive Statistics

	Repeat Intravenous Insertions	Attempts per Event	Room Time per Event	Phlebitis Scale 1-5	Infiltration Scale 1-5	Minutes Dose Delayed
Other antibiotic						
Mean	0.99	0.78	9.08	0.11	0.06	8.89
Median	1	1	10	0	0	0
Minimum	0	0	0	0	0	0
Maximum	9	4	60	2	2	360
N	104	104	104	104	104	104
Vancomycin						
Mean	1.47	1.12	14.90	0.08	0.20	13.57
Median	1.00	1.00	10.00	0.00	0.00	0
Minimum	0	0	0	0	0	0
Maximum	4	3	45	1	2	300
N	49	49	49	49	49	49
Total/all						
Mean	1.14	0.89	10.94	0.10	0.10	10.39
Median	1.00	1.00	10.00	0.00	0.00	0
Minimum	0	0	0	0	0	0
Maximum	9	4	60	2	2	360
N	153	153	153	153	153	15

information from the patient record augmented the study unit's data. Collection stopped when the patient received a central catheter insertion, when the antibiotics were discontinued, or the patient was discharged from the hospital. To increase the amount and accuracy of the data, the researcher verified the research tool's recorded data with the information found in the patient's records.

Statistical Analysis

Data were entered into SPSS® version 17 software. Numerical and categorical variables were summarized, and a series of analyses of variance (ANOVAs) were run on each outcome, comparing the vancomycin group to the group receiving other antibiotics. Regression analyses were performed on the outcomes to determine whether there was an interaction effect with total doses of antibiotics or average doses of antibiotics per day.

RESULTS

After 6 months of data collection, 153 patients met the criteria for the study. Patients (n = 153) were adults 18 years or older, roughly half women and half men, who had undergone orthopedic or gastrointestinal procedures or had experienced trauma to their body, such as a gunshot or stab wound, motor vehicle accident, or fall. Forty-nine patients received vancomycin, and 104 received only other antibiotics (Table 1). Of the 49 patients with PIV catheters receiving any vancomycin, 16 (33%) ended the study with a central catheter versus 15 (14%), and patients receiving other antibiotics ended the study with a central catheter.

Most patients had 1 additional peripheral venipuncture, with an average of 1.13 repeat venipunctures. Most venipunctures required 1 attempt, with mean room time of 10.94 minutes per event. Delayed doses averaged 10.39 minutes; however, the mode was zero, showing that most patients had no delay in the administration of a dose. The phlebitis and infiltration scores ranged from 0 to 2, with most antibiotics having neither of the complications. The vancomycin group actually had a maximum phlebitis score of 1 versus 2 for other antibiotics. The patients averaged a total of 16 doses of antibiotics, with a mode of 13 doses and 3.6 average doses per day (Table 2). During the 6 months of data collection, 1 patient developed a BSI; this patient had a central catheter insertion and was administered with multiple antibiotics, including vancomycin, as well as an extended stay in the hospital.

ANOVA was chosen to compare group means rather than using *t* tests. A *t* test also compares means, but running a series of *t* tests creates a greater chance of type I error, showing significance when there is none. ANOVA evaluates the treatment effect and error between the groups as well as within the groups; a significant value ($p < .05$) means that there is a low probability that the results occurred by chance and a high probability that the results are due to the intervention (ie, vancomycin in this study). Significant differences included insertions ($p = .038$), number of attempts ($p = .018$), nursing time in room ($p = .005$), and infiltration ($p = .020$). Phlebitis ($p = .683$) and minutes dose delayed ($p = .562$) were not significant contributors to the analysis (Table 3).

Linear regression analyses were run on each of the outcomes, with total antibiotics and number of doses per day as possible interactions (Table 4). While total number of doses could predict the number of repeated venipunctures ($p = .000$), there was also a significant interaction effect with vancomycin administration ($p = .017$). The number of attempts at PIV insertions was significant ($p = .028$) with vancomycin, despite

TABLE 2
Average and Total Doses

	Total Doses Given	Average Doses in a Day
Median	13.00	3.00
Mode	9	3
SD	15.96	1.45
Minimum	3	1
Maximum	154	9

TABLE 3
ANOVA Results of Outcomes

	Vancomycin vs Other	
Outcomes	*F*	*p*
Times repeat venipunctures needed	4.384	.038
Intravenous attempts at venipunctures	5.755	.018
Nurses' room time per event	8.231	.005
Phlebitis scale 1-5	0.167	.683
Infiltration scale 1-5	5.495	.020
Minutes dose delayed	0.338	.562

TABLE 4

Results of Regression

Interaction Effects	Standardized Coefficients, β	*t*	*p*
Total doses and average dose per day		0.964	.337
Any vancomycin	.167	2.424	.017
Average doses in a day	−.102	−1.259	.210
Total doses given	.596	7.531	.000
Repeat venipunctures		0.964	.337
Any vancomycin	.167	2.424	.017
Average doses in a day	−.102	−1.259	.210
Total doses given	.596	0.964	.337
Attempts		2.135	.034
Average doses in a day	.033	0.343	.732
Total doses given	.142	1.520	.131
Any vancomycin	.180	2.214	.028
Nurses' room time		1.111	.268
Average doses in a day	.071	0.752	.453
Total doses given	.095	1.019	.310
Any vancomycin	.210	2.593	.010
Phlebitis		1.613	.109
Average doses in a day	−.022	−0.228	.820
Total doses given	−.002	−0.022	.982
Any vancomycin	−.029	−0.342	.733
Infiltration		−0.293	.770
Average doses in a day	.008	0.083	.934
Total doses given	.011	0.119	.905
Any vancomycin	.185	2.249	.026
Minutes dose delayed		1.121	.264
Average doses in a day	−.054	−0.547	.585
Total doses given	−.017	−0.179	.858
Any vancomycin	.059	0.702	.484

average doses per day (p = .879) or total doses given (p = .157); there was no interaction effect. The time nurses spent in the room restarting a PIV catheter was significantly more for patients receiving vancomycin (p = .010), and there was no significant interaction effect with total doses or average doses. Infiltration scores continued the same trend and were significantly increased (p = .026) with any vancomycin administration. Phlebitis scores, however, were not significantly different in any of the groups.

DISCUSSION

The data supported nursing perceptions that vancomycin administration increased the number of venipunctures, number of attempts, and time spent restarting PIV catheters. The vancomycin group (n = 49) failed to meet the requirements of the power analysis (n = 64) but showed significant results despite the small sample size and data with small ranges. The findings may reveal that complications are real problems that show up even in small groups.

Nurses' initial observations were verified; they spent more time in the room and attempted more venipunctures in patients with vancomycin therapy. Each data point called an "attempt" or "room time" meant minutes spent looking for a vein, calling another nurse to look, turning on lights in the middle of the night, or phoning to find more experienced IV therapy nurses. Not only did venipunctures affect the patients, they also interrupted nursing workflow.

The interaction effects in the regression analysis revealed that total doses of any antibiotic, whether it was vancomycin or not, stood out as the primary predictor of the number of PIV insertions needed. Vancomycin administration contributed significantly to increased number of venipunctures, however. Even when total doses and average doses a day were factored into the regression equation, attempts, room time, and infiltration showed up as significant adverse outcomes in the vancomycin group.

TABLE 5

Study Antibiotics' pH[a]

Antibiotic	pH
Acyclovir	10.5-11.6
Ampicillin	8.0-10.0
Aztreonam	4.5-7.0
Cefazolin	4.5-6.0
Cefepime	4.0-6.0
Cefotaxime	5.0-7.5
Cefotetan	4.5-6.5
Cefoxitin	4.2-7.0
Ceftazidime	5.0-8.0
Ceftriaxone	6.7
Clindamycin	5.5-7.0
Daptomycin	Adjusted
Doripenem	4.5-5.5
Ertapenem	7.5
Erythromycin	6.5-7.5
Imipenem/cilastatin	6.5-8.5
Levofloxacin	3.8-5.8
Meropenem	7.3-8.3
Metronidazole	4.5-7.0
Micafungin	5.0-7.0
Oxacillin	6.0-8.5
Rifampin	7.8-8.8
Ticarcillin	5.5-7.5
Trimethoprim/sulfamethoxazole	9.5-10.5
Vancomycin	3.9

[a]*Data from Gordon.*[17]

Although other studies have shown phlebitis to be the greatest complication with vancomycin and PIV insertions, this study failed to confirm these results. Perhaps carrying out the study led to close monitoring and earlier detection of complications. Although the staff nurses thought cost could be an issue, most patients needed only 1 or 2 more PIV insertions after the original venipunctures before they were discharged from the hospital. Even if the PIV supplies and nursing time cost $45, it would take at least 7 total attempts to equal the cost of a nurse-led PICC insertion at $350. There are other reasons to insert a central catheter; it appears cost saving is not one of them.

Limitations to the study include sample size and ability to generalize findings to other units. Originally, the nurses considered a study design with 4 groups of patients with peripheral access receiving antibiotics ($pH < 4$) versus patients with peripheral access receiving antibiotics ($pH > 4$), as well as 2 groups with central catheters. However, the unit's study had no complications in the central catheter groups except the 1 BSI found after 6 months, so the study was changed to a 2-group design. Randomization was not done because each value was essential for the power analysis. Another issue was that vancomycin was the only antibiotic administered during the study period that met the pH less than 4 criterion, using the values for pH taken from Trissel's *Handbook on Injectable Drugs* (Table 5).[18] One of the major limitations was carrying out a study on a busy patient care unit. Data collection depends on nurse buy-in and agreement to set accurate documentation as a priority. As anticipated, specific concerns arose during the study, including loss of data for the "time in room" during starting of PIV catheters. Fifty-eight of the 100 repeat insertions used the 10-minute default value.

Furthermore, patient population, age, severity of illness, length of therapy required, and urgency of treatment and skill of the nurse inserting the IV catheter should also be considered.[12] Although all nurses in this study were qualified by the hospital to start PIV catheters, expertise was not quantified; future studies should include a measure for skill level. Finally, having all the nurses record observations is an interrater reliability issue that should be considered in a future study.

An interesting, unexpected event was the increase in central catheter insertion during the study. The findings that 33% of the vancomycin group patients received a central catheter may have reflected increased awareness of problems in long-term therapy. The unit's posters and flyers reminding nurses to record data brought the vancomycin concerns to the forefront of the physician's agenda. Whether it was just the subliminal suggestion, a type of Hawthorne effect, or the fear of negative publicity, orders for central catheters appeared sooner and more frequently than prior to the study. Had this been anticipated, data would have been collected on this phenomenon. It impacted the study by reducing the sample size of PIV insertions in the vancomycin group.

CONCLUSION

When faced with a patient who will undergo vancomycin therapy, clinical nurses are in a position to recommend central catheter or PIV insertion. This study's findings suggest that there are adverse outcomes with PIV vancomycin administration that contribute to vascular depletion. These included number of venipunctures, number of attempts, and higher infiltration scores. For nurses, this means more time spent inserting PIV catheters. Selection of the IV catheter should be methodically thought out to determine what is best for a patient's specific circumstances.

Although the cost of supplies and risk of complications are important factors to consider, early central catheter placement saves the patient from repeated PIV insertions or attempts at venipunctures as well as complications of infiltration. Giving medications to a patient with a central catheter saves time and minimizes interruption of a nurse's work with reinserting a PIV catheter. Asking questions on admission or when care changes due to access issues would benefit the patient and caregivers. Of concern are the total number of doses of antibiotics and whether or not vancomycin can be substituted for other antibiotics. Providing patients with information regarding the benefits and risks of central catheters versus peripheral catheters based on care needs is an opportunity to involve the patient in the care to be delivered. The nurse plays a critical and escalating role in using holistic and outcome-driven recommendations that will benefit the patient.

ACKNOWLEDGMENTS

The authors thank the nurses on 5 Bedtower for their input and dedication to the unit's first research project.

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